

### I. The Office Action

The December 28, 2006 final Office Action (the "Office Action") in this application:

- 1.) objects to claim 35;
- 2.) rejects claims 11 and 35-40 under 35 U.S.C. 112, first paragraph;
- 3.) rejects claims 11, 34, 35 and 36-38, 40-42 and 44 under 35 U.S.C. 103(a);  
and
- 4.) rejects claims 11 and 34-44 under 35 U.S.C. 103(a).

Applicants respond as follows and hereby petition for a request for continued examination (RCE).

### Remarks

Applicants note that in the Office Action of December 14, 2006, then pending claims 11 and 34-35 were found to be allowable (Office Action Summary and page 6 of the Office Action of December 14, 2006). In order to place the application in condition for allowance and in response to the Office Action, Applicants cancelled all other claims that were asserted to be non-allowable, to provide for expedited prosecution and thus placed the application in condition for allowance. However, another non-final Office Action was then issued, which rejected the previously allowed claims, which then necessitated the filing of a further reply by the Applicants, which then resulted in the issuance of the currently outstanding Final Office Action.

## II. Amended claims and Priority

Claims 11 and 35 are hereby amended by this submission. Support for “causing the regression or remission” recited in amended claim 11 can be found at least at page 31, line 12 of the specification, for example. Claim 35 is amended to now depend from claim 11, instead of from cancelled claim 12.

In reviewing documents from which priority is claimed, applicants respectfully point out that applicant’s specification need not describe the claimed invention *ipsis verbis* in order for priority to be claimed. Applicants submit that the disclosure reasonably conveys to a person having ordinary skill in the art that the applicant had possession of the subject matter later claimed. For example, in the instant specification, atypical tissues include hyperplastic tissues and neoplasms, types of tissues that were recited in documents from which priority is claimed. It is also note, for example, that a botulinum toxin implant is also recited on page 17 of 10/631,221. Therefore, applicants note that priority for the pending claims is earlier than the instant application, and respectfully request the Examiner to note same.

III. Objection of claim 35

The Office Action has objected to claim 35, for depending from cancelled claim 12. Claim 35 has been amended to depend from pending claim 11, and thereby this objection is overcome.

Thus, this rejection should be withdrawn.

IV. Rejection of claims 11 and 35-40 under 35 U.S.C. 112, first paragraph

The Office Action has rejected claims 11 and 35-40 under 35 U.S.C. 112, first paragraph because the specification, while being enabling for a method of for treating a mammary gland disorder, which is an atypical tissue with botulinum toxin type A, does not reasonably provide enablement for preventing development of an atypical tissue, thereby treating the mammary gland. Applicants respectfully traverse this rejection.

In considering the rejection of the Office Action, it appears that the rejection is based upon the assertion that one of ordinary skill in the art cannot extrapolate teachings of the instant invention to enable a method of preventing the development of an atypical tissue (page 3 of the Office Action). Further, the Office Action asserts that there is no guidance in the specification as to how to determine and select a population of individuals which may or may not eventually have cancer (page 4 of the Office Action), while at the same time stating that it is well known that clinicians screen candidates for possible prevention, but then stating that even these screening procedures are not fool proof (page 4 of the Office Action), a point which is unrelated to the pending claims or patent prosecution (being "fool proof" is not a question related to a determination of patentability of an invention). Applicants note that the instant specification discloses that it is known to utilize various morphological markers (including precancerous breast tissue, e.g. various hyperplasias) as indicators of a patient's potential risk of developing breast cancer (see page 4, lines 5-19 of the specification, for example), however, these issues are not relevant to the instant claims, as discussed below.

It appears that based upon various assertions made in the Office Action, the meaning of the recited claim term "prevent the development of atypical tissue" has been misconstrued and taken out of the context of the application as a whole. According to discussions in the Office Action regarding population

screening, determination of a population of subjects in which cancer could be prevented, determination of susceptible cancer candidates from a population, discussion of vaccines and elicitation of immune responses and inapplicability of the vaccine approach to cancer therapy (pages 4-5 of the Office Action), that seems that the Office Action is taking the claim term "prevent the development of atypical tissue" to encompass administration to patients that are healthy and to prevent development of normal tissue into atypical tissue. This is not the case.

As utilized in the specification and as claimed, the claimed method treats a mammary gland disorder (as recited in independent claims 11 and 34), that is, the method is limited to and is applicable to patients already having a mammary gland disorder, i.e. that have atypical tissue (page 1, lines 18-25 of the specification). As discussed in the instant specification, the present invention encompasses methods for treating atypical tissues, such as hyperplastic tissues, cysts and neoplasms (including tumors and cancers) and for preventing the development of, or for causing the regression or remission of, atypical tissues, cysts and neoplasms. For example as disclosed as one aspect of the teachings of the disclosure, administration of botulinum toxin causes a reduction in the size and/or activity of a hyperplastic, hypertonic or neoplastic mammary gland tissue. For example and in one aspect disclosed in the specification, the method for preventing development of a neoplasm can comprise the step of local administration of a botulinum toxin to a hyperplastic tissue, thereby preventing development of the hyperplastic tissue into a neoplasm.

Thus, use of the term "prevent development", as claimed and as described in the specification, is not directed to administration of botulinum toxin to subjects in a population that do not have a mammary gland disorder, but rather (and as clearly recited in the pending claims) to patients that already manifest atypical tissue, the administration preventing the further development of the atypical tissue into, for example, a neoplasm.

In order to more particularly point this out, claim 11 has been amended such that "prevent the development of atypical tissue" has been replaced by "cause the regression or remission of atypical tissue", which should make clear the regressive/remissive teachings of utilization of botulinum toxin to inhibit the further development of atypical tissue, such as into a neoplasm, for example. That is, there is no undue experimentation necessary for one of ordinary skill in the art to practice the instant claimed invention, as the claims themselves make clear that those to be treated already have a mammary gland disorder, and thus discussion of population screening and other related aspects presented in the Office Actions regarding selection of subjects are moot.

Regarding the Office Actions discussion regarding xenograft models (Gura et al. Science 278:1041-1042 Nov 7, 1997), they nor the teachings of Gura et al. do not appear to be relevant or related to the instant claims.

Thus, this rejection should be withdrawn, and Applicants respectfully request allowance of claims 11 and 34 (previously allowed) and claims dependant therefrom.

V. Rejection of claims 11, 34, 35, and 36-38, 40-42 and 44 under 35 U.S.C. 103(a)

The Office Action rejects claims 11, 34, 35, and 36-38, 40-42 and 44 under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent Application Publication 2001/0043930 A1 and in further view of Wald and Klaus (The Australian and New Zealand Journal of Surgery 33(3): 200-204, February 1964). Applicants traverse this rejection.

Applicants maintain their previous arguments made in their reply of Oct. 2, 2007. From a review of the assertions made on page 7 of the Office Action, it appears that the Office Action has misconstrued the teachings of the Wald and Klaus document, stating (page 7, lines 18-20 of the Office Action) that in the Office Action's purview, the substance of the apocrine glands "is a mucus secretion", which is the basis of the Office Action's combination of the two cited documents (page 7, lines 20-21 of the Office Action).

The Office Action provides no basis for this purview, and indeed such a purview is incorrect. Wald and Klaus do not disclose that apocrine glands secrete mucus, and further does not mention and is completely silent regarding any use of botulinum toxin (instead referring to excision and an X-ray regime to treat the carcinoma, as known in the 60's), let alone to treat a mammary gland disorder. Wald and Klaus specifically teach and state that apocrine glands are "odoriferous or accessory sex glands", (page 203, left column, fourth through sixth full paragraphs) where it is described that they elaborate a definite substance *which itself has a role in the primitive animal physiology* (emphasis added). This clearly refers to the odiferous secretions of the apocrine glands (pheromones, not mucus). Indeed, as stated in Wald and Klaus and agreed to by the Office Action, apocrine glands are not sweat glands.

Applicants respectfully point out that and remind the Office that mucus is a slippery secretion that lines mucous membranes in the body and is made up of mucins. Exemplary mucus membranes can be found in the digestive and a respiratory tract, where the secretion of mucus provides lubrication of foodstuffs' passage (digestive tract) and is used to trap pathogens and prevent infection (respiratory and digestive tracts).

Thus, when taking the teachings of Wald and Klaus as a whole and in their proper context, the basis for the Office Action's combination of the two cited documents does not exist. We note again that there is no discussion or hint of botulinum toxin use in Wald and Klaus, and there is no discussion in U.S. Patent Application Publication 2001/0043930 A1 regarding the treatment of mammary gland disorders, particularly cancerous disorders. Thus, the combination of the two documents is based upon the Office Action's misconstruction that the secretions of apocrine glands are mucus, instead of the odoriferous secretion (pheromone), as detailed in Wald and Klaus. The combination of documents is then simply an exercise in hindsight reconstruction, since U.S. Patent Application Publication 2001/0043930 A1 does not disclose utilizing botulinum toxin to treat mammary gland disorders or pheromones for that matter, and Wald and Klaus are silent as to any treatment of apocrine carcinoma other than surgical excision and X-ray irradiation.

Thus, this rejection should be withdrawn.



VI. Rejection of claims 11, 34-44 under 35 U.S.C. 103(a)

The Office Action rejects claims 11, and 34-44 under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent Application Publication 2001/0043930 A1 and in further view of Wald and Klaus (The Australian and New Zealand Journal of Surgery 33(3): 200-204, February 1964) and U.S. Patent No. 6,312,708. Applicants traverse this rejection.

For at least the reasons provided above, the basis for rejecting claims 11, and 34-44 under 35 U.S.C. 103(a) is improper, and is not remedied by U.S. Patent No. 6,312,708, which is directed to controlled release systems for release of therapeutic amounts of botulinum toxin.

Thus, this rejection should also be withdrawn.

VII. Conclusion

All issues raised in the Office Action have been addressed. Only claims 11, 34-44 remain, which are in condition for allowance. Accordingly, a notice of allowance to that effect is respectfully solicited.

Should any matter(s) remain unresolved, the Examiner is invited to call Claude L. Nassif at the number below.

The Commissioner is hereby authorized to charge any fee(s) required or necessary for the filing, processing or entering of this paper, including the fees necessary for requesting continued examination (RCE) or any of the enclosed papers and to refund any overpayment to deposit account 01-0885.

Respectfully submitted,

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